REMARKS

Claims 11-14 have been cancelled, as drawn to the non-elected invention. Claims 1-10 are currently under examination in the present application. Claims 2-7 have been cancelled. Claim 1 has been amended. No new matter has been added. Applicants reserve the right to refile this subject matter in a continuation or divisional application filed during the pendency of this application.

Claim Objection

Claim 2 was objected to as being of improper dependent form for failing to further limit the subject matter of a previous claim. Specifically, the claim was objected to because there are no other possible orientations and thus has the same scope as claim 1, not further limiting claim 1. Claim 2 has been cancelled, thereby rendering the objection moot.

Rejection under 35 U.S.C. § 112(1)

Claims 1-2 and 4-10 were rejected under 35 U.S.C. § 112 (1) as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey of one skilled in the art that the inventor at the time the application was filed had possession of the claimed invention. The claims are drawn to a method to reduce transcriptional interference between two or more tandemly arranged gene expression cassettes in a host cell comprising having a spacer polynucleotide between the cassettes, which spacer polynucleotide results in a reduction of transcriptional interference. There is no limitation on what the spacer can be; only that it functions to reduce transcriptional interference. Thus, the method claims are genus claims because the spacers are a genus of polynucleotides only defined by function.

Claims 2 and 4-7 have been cancelled, thereby rendering the rejection of these claims moot. Claim 1 has been amended to recite the specific sequences, previously recited in claim 3, which the spacer polynucleotide can comprise, thereby limiting and defining the spacer polynucleotide. Applicants contend that claim 1 and dependent claims 8-10 satisfy the written description requirement of 35 U.S.C. § 112(1). Thus, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 112(2)

Claims 1-10 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the examiner indicating that the recitation of "interference between two or more tandemly arranged gene expression cassettes" renders the claims vague and indefinite because the claim only recites one spacer between two cassettes; there is no indication of more than two

cassettes nor is there an indication of more than one spacer for the additional spaces between the additional cassettes.

Claims 2 and 4-7 have been cancelled, thereby rendering the rejection of these claims moot. Claim 1 has been amended to recite only "interference between two tandemly arranged gene expression cassettes," thereby obviating the basis for the rejection of claims 1 and 8-10. Accordingly, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(b)

Claims 1-2 and 4-10 were rejected under 35 U.S.C. § 102(b) as anticipated by Eggermont *et al.* Eggermont *et al.* teach introduction into a host human cell two tandemly arranged gene expression cassettes, each driving the expression of a truncated human alpha2 globin gene. The reference teaches that the two expression cassettes interfere with the expression of each other, which expression interference is alleviated by insertion of a poly(A) signal or a transcriptional pause site or both between the expression cassettes. Although the actual A/T content is not taught, claims 4-7 are drawn to the spacer polynucleotide comprising at least up to 63% A/T content, which is open language, and thus if only a part of the poly(A) signal and/or transcriptional pause site is A/T rich, then it meets the claim limitations because the claims are open to the rest of the element being low in A/T content.

Claims 2 and 4-7 have been cancelled, thereby rendering the rejection of these claims moot. Claim 1 has been amended to recite the specific sequences, previously recited in claim 3, which the spacer polynucleotide can comprise. Eggermont *et al.* do not teach introduction of spacer sequences comprising nucleic acid sequences comprising SEQ ID NO: 1, 2 3 or 4. Applicants contend that claim 1 and dependent claims 8-10 are not taught or anticipated by Eggermont *et al.* Thus, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 1-2 and 4-10 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Ingelbrecht *et al.* The examiner suggests that Ingelbrecht *et al.* teach introduction into a host cell a construct made by insertion of a poly(A) signal/terminator between two tandemly arranged gene expression cassettes blocks readthrough which restores the expression of the gene in. The poly(A) signal/terminator reads on a spacer nucleotide because it reduces the transcriptional interference. Although the actual A/T content of the spacer is not taught, claims 4-7 are drawn to the spacer polynucleotide comprising at least up to 63% A/T content, which is open language and thus if only a part of the poly(a) signal/terminator is A/T rich, then it meets the claim limitations because the claims are open to the rest of the element being low in A/T content. The cell taught for the method is

tobacco. At least one of the gene expression cassettes is nptII, which at least reads on an antigen because essentially all polypeptides are antigens. This reference teaches "using chimeric gene constructs we demonstrate that transcriptional activity interferes with the expression of a downstream gene in opposite orientation in transient expression and is much more pronounced in transgenic plants...A poly(A) signal/terminator can substantially reduce readthrough from the upstream promoter, and thereby alleviate this interference."

Claims 2 and 4-7 have been cancelled, thereby rendering the rejection of these claims moot. Claim 1 has been amended to recite the specific sequences, previously recited in claim 3, which the spacer polynucleotide can comprise. Ingelbrecht *et al.* do not teach introduction of a spacer between expression cassettes in which the spacer sequence comprises nucleic acid sequences comprising SEQ ID NO: 1, 2 3 or 4. Applicants contend that claim 1 and dependent claims 8-10 are not taught by Ingelbrecht *et al.* Thus, withdrawal of the rejection is respectfully requested.

Applicants respectfully request reconsideration and withdrawal of all of the above rejections in view of the above arguments and the presently pending claims.

Respectfully submitted,

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